Point of view

Redefining transient ischaemic attack

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Sri Lanka Journal of Neurology, 2012, **1**, 39-40

Index words: transient ischaemic attack (TIA), stroke, ABCD^2 score

Around 23% of patients with ischaemic stroke give a history of preceding transient ischaemic attack (TIA)[1,2] whilst TIAs occurred most often in the 48 hours to 2 weeks prior to the presenting stroke[2]. TIA is associated with high risk of early recurrent stroke[3] with stroke rates as high as 35% in some subgroups by 7 days[4]. The window between TIA and stroke is often hours to days and preventive interventions initiated urgently after TIA can substantially reduce the risk of stroke. Antiplatelet agents[5,6], antihypertensive drugs[7], statins[8], anticoagulation (in atrial fibrillation or intracardiac thrombi)[9] and carotid endarterectomy (for symptomatic carotid stenosis)[10] have shown to prevent stroke after a TIA. The ABCD^2 score [age (≥60 years = 1 point); blood pressure elevation when first assessed after TIA (systolic ≥140 mmHg or diastolic ≥90 mmHg = 1 point); clinical features (unilateral weakness = 2 points; isolated speech disturbance = 1 point; other = 0 points); duration of TIA symptoms (≥60 minutes = 2 points; 10 to 59 minutes = 1 point; <10 minutes = 0 points); and diabetes (present = 1 point)] is widely used to stratify the early stroke risk after TIA[4].

TIA has been traditionally defined as an acute loss of focal brain or monocular function with symptoms lasting less than 24 hours and which is thought to be due to inadequate cerebral or ocular blood supply. The 24-hour threshold used to distinguish TIA from stroke is arbitrary and arose in the mid-1960s[11]. At that time, it was assumed that transient symptoms disappeared completely because no permanent brain injury had occurred. However, with the advent of advanced imaging techniques such as diffusion-weighted MRI studies, it has been demonstrated that up to a third of ischaemic episodes with symptoms lasting only 24 hours or less were also associated with brain infarction[12]. This has led to the proposal of a revised definition of TIA as a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction[13]. This is a tissue-based definition that relies on excluding end-organ damage (ie, infarction) rather than the arbitrary time limit specified in the original definition. The new definition takes into account that infarction can occur irrespective of the duration of the transient neurological symptom. Although the clinical symptoms of TIA typically last less than one hour, a systematic analysis has shown that symptom duration is not a reliable predictor for the presence of infarction[14]. The new definition entails the need for brain imaging (ideally, diffusion-weighted magnetic resonance imaging – DWI) in the acute phase.

Should the time-based clinical definition of TIA be replaced by the new tissue-based definition that incorporates brain imaging?

Several studies have shown that the presence of infarction, particularly on DWI, is associated with a higher risk of stroke in patients clinically presenting with a time-defined TIA[12,15,16]. The 7-day stroke risk among patients with acute infarction on DWI (7.1%) was 18-fold higher than those without acute infarction (0.4%). Furthermore, it has been shown that incorporation of brain infarction into the ABCD^2 score (ABCD^2-I) improves the prediction of stroke after TIA[12,15,16].

Although the presence of infarction is the major determinant of early stroke, the ABCD^2 score has predictive value in the acute phase in both tissue-positive and tissue-negative patients, identifying individuals at higher and lower risk within both these groups[15]. A high ABCD^2 score in patients presenting with a time-defined TIA, irrespective of whether tissue-positive or -negative, warrants early intervention to prevent stroke. Moreover, unstable vascular disease factors known to be associated with a high risk of stroke after TIA such as carotid stenosis and atrial fibrillation require early intervention in all patients presenting with a time-defined TIA. The advantage of the ABCD^2 system is that it has been designed as an initial assessment tool in a primary care / emergency setting based purely on clinical parameters. The identification of a brain infarct only refines the risk prediction of recurrent stroke.

The time-based definition of TIA, although arbitrary, has served the clinician well in recognising a neurovascular syndrome that provides an opportunity to prevent stroke. The ABCD^2 score augments this definition by providing a reliable clinical prediction tool to guide the clinician in prognostication and treatment of individual patients. In comparison, the recently proposed tissue-based definition of TIA utilises DWI in identifying a subcategory of time-defined TIA as true TIA with a relatively lower risk of stroke on the basis of absent brain infarction. However, the tissue-based definition has the

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disadvantage of requiring advanced imaging facilities in an acute setting.

It is therefore sensible to retain the time-based definition of TIA. It is simple and reliable. Where brain imaging facilities are available, time-defined TIA can be categorized as *with-infarction* and *without-infarction* to provide prognostic information. This classification recognizes that the clinical syndrome of TIA lasting less than 24 hours can occur with or without brain infarction, and that the latter carries a higher risk of early recurrent stoke. The $ABCD^2$ score should be used to refine the risk of stroke in both tissue-positive and -negative TIA, and to predict the risk of stroke after TIA when brain imaging is unavailable.

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